AMENDMENTS TO THE CLAIMS

The following Listing of the Claims replaces all prior claims in the application.

Claim 1 (Original). A transgenic non-human mammal whose genome comprises a transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous amyloid precursor protein 695 (APP_{695}) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and wherein the transgene is expressed.

Claim 2 (Original). The transgenic mammal of claim 1 wherein the mammal is a mouse.

Claim 3 (Original). The transgenic mouse of claim 2 wherein the mouse is a (C3H x C57 BL6) x C57 mouse.

Claim 4 (Original). The transgenic mouse of claim 3 wherein the heterologous APP_{695} is human APP_{695}.

Claim 5 (Original). The transgenic mouse of claim 4 wherein the mouse displays abnormal Aβ deposition in its central nervous system.

Claim 6 (Currently Amended). The transgenic mouse of claim 4 wherein the animal displays an ~~accelerated~~ appearance of Alzheimer's Disease-related pathology by 3 months of age.

Claim 7 (Currently Amended). A ~~transgenic~~ mouse having the transgenic mouse of claim 4 as an ancestor, wherein the mouse comprises said transgene.

Claim 8 (Withdrawn). A transgenic non-human mammal produced by:

(a) crossing a first transgenic non-human mammal in accordance with claim 1 with a second non-human mammal having a genome comprising a second gene

comprising a nucleotide sequence operably linked to a promoter and encoding a selected protein having at least one selected mutation to produce first generation offspring; and

(b) selecting from the first generation offspring a transgenic non-human mammal having a genome comprising at least one first transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous APP_{695} polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and at least one second gene comprising a nucleotide sequence operably linked to a promoter and encoding said selected protein having at least one selected mutation and expressing both said at least one first transgene and said at least one second gene.

Claim 9 (Withdrawn). The transgenic non-human mammal of claim 8 wherein the selected protein is a presenilin and the selected mutation is an AD-related mutation.

Claim 10 (Withdrawn). The transgenic non-human mammal of claim 8 wherein the selected protein is selected from the group consisting of a low density lipoprotein receptor related gene, an α2-macroglobulin gene and a β-secretase gene and the selected mutation is an Aβ processing-related mutation.

Claim 11 (Withdrawn). The transgenic non-human mammal of claim 10 wherein the mammal is a mouse.

Claim 12 (Withdrawn). A transgenic mouse produced by:

(a) crossing a first transgenic mouse in accordance with claim 4 with a second mouse having a genome comprising a second gene comprising a nucleotide sequence operably linked to a promoter and encoding a selected protein having at least one selected mutation to produce first generation offspring; and

(b) selecting from the first generation offspring a transgenic mouse having a genome comprising at least one first transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous APP_{695} polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and at least one second gene comprising a nucleotide sequence operably linked to a promoter and encoding said selected protein having at least one selected mutation and expressing both said at least one first transgene and said at least one second gene.

Claim 13 (Withdrawn). The transgenic mouse of claim 12 wherein the second gene is a mutant endogenous gene.

Claim 14 (Withdrawn). The transgenic mouse of claim 12 wherein the second gene is a transgene.

Claim 15 (Withdrawn). The transgenic mouse of claim 12 wherein the second gene comprises a nucleotide sequence encoding a selected protein having an AD-related amino acid substitution.

Claim 16 (Withdrawn). The transgenic mouse of claim 15 wherein the selected protein is a presenilin.

Claim 17 (Withdrawn). The transgenic mouse of claim 12 produced by:

(a) crossing a first transgenic mouse in accordance with claim 4 with a second transgenic mouse having a genome comprising a transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 2 polypeptide wherein the methionine residue at position 239 is substituted by valine to produce first generation offspring; and

(b) selecting from the first generation offspring a transgenic mouse having a genome comprising at least one first transgene comprising a nucleotide

sequence operably linked to a promoter and encoding a heterologous amyloid precursor protein (APP) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and at least one second transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 2 polypeptide wherein the methionine residue at position 239 is substituted by valine and expressing both said first and second transgenes.

Claim 18 (Withdrawn). The transgenic mouse of claim 12 produced by:

(a) crossing a first transgenic mouse in accordance with claim 4 with a second transgenic mouse having a genome comprising a transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 1 polypeptide wherein the leucine residue at position 286 is substituted by valine to produce first generation offspring; and

(b) selecting from the first generation offspring a transgenic mouse having a genome comprising at least one first transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous amyloid precursor protein (APP) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and at least one second transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 1 polypeptide wherein the leucine residue at position 286 is substituted by valine and expressing both said first and second transgenes.

Claim 19 (Withdrawn). The transgenic mouse of claim 12 produced by:

(a) crossing a first transgenic mouse in accordance with claim 4 with a second transgenic mouse having a genome comprising a transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 1 polypeptide wherein the methionine residue at position 146 is substituted by

leucine and the leucine residue at position 286 is substituted by valine to produce first generation offspring; and

(b) selecting from the first generation offspring a transgenic mouse having a genome comprising at least one first transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous amyloid precursor protein (APP) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and at least one second transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 1 polypeptide wherein the methionine residue at position 146 is substituted by leucine and the leucine residue at position 286 is substituted by valine and expressing both said first and second transgenes.

Claim 20 (Withdrawn). A method for screening a candidate compound for its efficacy in preventing or delaying the development of AD, the method comprising the steps of:

(a) administering the candidate compound to a first transgenic mouse in accordance with any one of claims 1 to 19 prior to the appearance of a selected AD-related phenotypic trait in said mouse; and

(b) comparing the age at which said selected AD-related phenotypic trait appears in said mouse with the age at which said trait appears in a second transgenic mouse of the same type to which the compound had not been administered;

wherein an increased age of appearance of the trait in the first mouse compared to that in the second mouse indicates efficacy of the compound.

Claim 21 (Withdrawn). The method of claim 20 wherein the trait is a behavioral deficit.

Claim 22 (Withdrawn).) The method of claim 20 wherein the trait is abnormal CNS amyloid deposition.

Claim 23 (Withdrawn). A method for screening a candidate compound for its efficacy in ameliorating the symptoms of Alzheimer's Disease, the method comprising the steps of:

(a) administering the candidate compound to a first transgenic mouse in accordance with any one of claims 1 to 19;

(b) determining the performance of said mouse in a memory or learning test; and

(c) comparing the performance of said mouse with the performance of a second transgenic mouse of the same type to which the compound has not been administered;

wherein an improved performance of the first mouse compared to that of the second mouse indicates efficacy of the compound.

Claim 24 (Original). A method of producing a transgenic non-human mammal that displays abnormal Aβ deposition in its central nervous system comprising:

(a) introducing into a fertilized oocyte of said mammal a transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous amyloid precursor protein 695 (APP_{695}) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine;

(b) transplanting said fertilized oocyte into a pseudopregnant mammal;

(c) allowing said fertilized oocyte to develop into a live born offspring; and

(d) selecting an offspring where genome comprises a transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous amyloid precursor protein 695 (APP_{695}) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and wherein the transgene is expressed.

Claim 25 (Original). The method of claim 24 wherein the mammal is a mouse.

Claim 26 (Original). The method of claim 24 wherein the promoter is the prion protein cos.Tet promoter.

Claim 27 (Original). A nucleotide sequence encoding a heterologous amyloid precursor protein 695 (APP_{695}) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine.

Claim 28 (Original). A vector comprising the nucleotide sequence of claim 27 operably linked to a promoter.

Claim 29 (Withdrawn). A method of reducing a cognitive deficit in a mammal which suffers from abnormal amyloid deposition in its central nervous system, the method comprising administering to the mammal an amount of an $A\beta$ peptide effective to reduce the cognitive defect.

Claim 30 (Withdrawn). The method of claim 29 wherein the abnormal amyloid deposition is Aβ deposition.

Claim 31 (Withdrawn). The method of claim 29 or 30 wherein the administered peptide is Aβ42.

Claim 32 (Withdrawn). The method of any one of claims 29 to 31 wherein the mammal is a human suffering from Alzheimer's Disease.

Claim 33 (Withdrawn). Use of an Aβ peptide to manufacture a medicament for reducing a cognitive deficit in a mammal which suffers from abnormal amyloid deposition in its nervous system.

Claim 34 (Withdrawn). The use of claim 33 wherein the Aβ peptide is Aβ42.

Claim 35 (Withdrawn). The use of claim 33 or 34 wherein the medicament is for the prevention or treatment of Alzheimer's Disease.